NSBRI Smart Medical Systems Team Strategic Plan

12.0 Smart Medical Systems

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12.1 INTRODUCTION

Health problems associated with space travel may be related to the effects of microgravity, radiation and other risks to the body that are particular to space flight. They may also be independent of these effects, arising in association with a given demographic population, toxic environmental exposure or trauma. Complex interactions between these factors, as well as potential differences in the way disorders present and respond in microgravity relative to Earth, pose formidable challenges. The unique medical circumstances and limited health care resources in space suggest that novel strategies are required for in-flight physiological monitoring and medical assessment, diagnosis and treatment on long duration missions.

The Smart Medical Systems Team (SMST) plans a leadership role in the research and development of an advanced, integrated and autonomous system for astronaut health assessment, maintenance and medical care. This includes the delivery and evaluation of medical interventions and other countermeasures to reduce the deleterious effects of space travel and enhance the overall well-being of astronauts. To accomplish this task, the SMST works closely with other NASA efforts in space and critical medicine. It is anticipated that the countermeasure program of the SMST will have significant impact and applications for Earth-based health and medical care.

12.2 RISKS

The following risks have been identified in the Critical Path Roadmap under Clinical Capabilities (risk number in parentheses).

- Trauma and Acute Medical Problems (43)
- Toxic Exposure (44)
- Altered Pharmacodynamics and Adverse Drug Reactions (45)
- Illness and Ambulatory Health Problems (46)
- Development and Treatment of Space-Related Decompression Sickness (47)
- Difficulty of Rehabilitation Following Landing (48)

12.3 GOALS

Risk-Based Goals: Development of Methods for Health Assessment and Medical Care

Goal 1: Methods to reduce risk of trauma and acute medical problems

Goal 2: Methods to reduce risk of toxic exposure

Goal 3: Methods to reduce risk of altered pharmacodynamics and adverse drug reactions

Goal 4: Methods to reduce risk of illness and ambulatory health problems

Non Risk-Based Goals

Goal 5: Develop a platform for suite of medical devices

Goal 6: Develop Earth-based applications for non-invasive, portable physiological sensing and medical diagnostic and therapeutic devices

Goal 7: Integrate research and analysis

12.4 DESCRIPTION AND EVALUATION OF CURRENT PROGRAM

The SMST was formed in 2000, and funded in 2001, following peer-review of applications for research to mitigate risks most closely associated with the Clinical Capabilities discipline of the Critical Path Roadmap as listed in Section 12.2. The emphasis has been on addressing the four highest priority risks (Goals 1 to 4) in the discipline, with the requirement that Goal 5 be developed to integrate the projects together as a prototypical smart medical system, that can be demonstrated and implemented. Achievements toward Goal 6 are already being realized, even though the team has only recently been established, and Goal 7 is partially addressed in Goal 5, as well as in other contexts described later.

Given the team's goals, collaborations have been essential. These have been initiated and fostered across the NSBRI and with NASA flight surgeons, astronauts, medical operations personnel, engineers and researchers at the Johnson Space Center (JSC). The team has also developed a working collaboration with biosensor and other groups at the Ames Research Center (ARC), the Jet Propulsion Laboratory (JPL) and other NASA Centers. It has engaged in a working relationship with the NASA Chief Health and Medical Officer.

Collaborations are a cornerstone for the team to meet its objectives and to strategically utilize its assets to help mitigate risks, especially those delineated in Goals 1 to 4. At present, the SMST has eight projects headed by seven principal investigators. Five projects (led by Drs. Crum, Davies, Klempner, Soller and Sutton) address research and development of novel biometric sensors that are lightweight, portable, low power, non-invasive and unobtrusive. These projects have applications for physiological and medical monitoring of astronauts, as well as for the assessment of countermeasures that potentially diminish the deleterious effects of long duration space travel (Goals 1, 2 and 4). Dr. Davies' project also has applicability to the risk of ameliorating the difficulty of rehabilitation following landing (currently a non-goal risk - Section 11.2). One project (led by Dr. Putcha) develops a novel pharmacological drug delivery system for near term countermeasure administration (Goal 3), while another project (led by Dr. Crum) develops a revolutionary new form of non-invasive surgery (Goal 1). A NASA echocardiographic resource project (led by Dr. Thomas) is supported by the SMST (Goals 1 and 4), and is jointly supervised with the Cardiovascular Alterations Team. Three projects (led by Drs. Klempner, Sutton and Thomas) develop "smart" algorithms for minimal user evaluation and interpretation of real time physiological and medical data (Goals 1 to 5 and Goal 7).

The current program consists of eight multi-disciplinary projects (3 animal, 1 human + animal, 2 human + computation, 1 pathogen, 1 resource) that integrate engineering, computation and biomedicine with innovation in technology and medical care. All of the projects fit within the objectives and strategic activities of the SMST (Section 12.5). Although the team is newly formed, there is preliminary planning for flight tests of some technologies, and for applying research discoveries to enhance medical care on Earth (Goal 6). A synopsis of the projects follows, with the major attributes being summarized in Table 11.1.

Crum et al.: Guided High Intensity Focused Ultrasound for Mission-Critical Care
This project seeks to develop a lightweight, portable, smart medical device that can adequately control internal bleeding, as well as address a number of other medical conditions that require surgery. This device will use diagnostic ultrasound for guidance and High Intensity Focused Ultrasound (HIFU) for therapy. Specifically, an image-guided transcutaneous device for acoustic hemostasis and bloodless surgery is proposed.
Countermeasure Target(s): Revolutionary surgical advance for use in trauma and for monitoring and assessment of other medical problems.

Davies et al.: Vascular Genomics in Gravitational Transitions
This ground-based project will address, at the level of gene expression, the structural and regulatory changes in murine vascular tissues associated with (a) exposure to simulated microgravity, (b) return to normal posture, and (c) prolonged exposure to hypergravity, and its acute reversal. Changes in RNA expression in regions of the vascular tree known to be of particular relevance to human orthostatic intolerance, and of critical importance in normal blood vessel regulation, will be investigated.
Countermeasure Target(s): Training and other interventions to minimize effects of vascular change, with pre-, in- and post-flight applications.

Klempner et al.: Smart Medical System for Microorganism Detection
This proposal involves the development of a novel smart medical system to detect and identify bacteria through the use of novel sensors and includes three steps: (a) development of "fingerprinting" phage display libraries which can detect, identify, quantify and discriminate bacterial species in environmental and biological specimens; (b) application of phage displayed peptides and antibody fragments in a microarray to the surface of a microsensor to demonstrate,

using optical readout and colorimetric reflectance, the sensitivity and specificity for detecting and discriminating between bacterial species using surface "fingerprints"; and (c) development of algorithms from the microarray response for real-time identification and discrimination of bacterial species.
Countermeasure Target(s): Novel monitoring and diagnostic capabilities with environmental manipulation and pharmacological countermeasure possibilities.

Putcha et al.: Microcapsule Gel Formulation for Intranasal Promethazine HCl
The goal of this project is to develop an intranasal dosage formulation of promethazine hydrochloride that will provide crewmembers with a non-invasive means of self-administering space motion sickness medications. The research involves the (a) development of a microencapsulated, pH-balanced gel dosage formulation and a combination form with a corticosteroid for intranasal administration, (b) establishment of release kinetics and shelf life of the optimized dosage forms, and (c) assessment of bioavailability, nasal mucosal irritability and toxicity of the selected dosage forms in rats.
Countermeasure Target(s): Novel drug delivery system for pharmacological agent administration.

Soller et al.: Noninvasive Measurement of Blood And Tissue Chemistry
This project uses near infrared spectroscopy and novel algorithms to non-invasively assess blood and tissue for the measurement of oxygenation, pH, glucose and hematocrit in humans, irrespective of skin color and gender. These parameters are important in diagnosing and treating hypoxia and trauma that may arise from exposure to radiation, toxic chemicals and blunt or sharp injury. They may also be useful in evaluating exercise as a countermeasure for extended weightlessness.
Countermeasure Target(s): Physiological and medical monitoring and diagnosis of blood and tissue parameters. Some parameters, such as muscle pH, are relevant for optimizing exercise countermeasures.

Sutton et al.: Near Infrared Brain Imaging for Space Medicine
This project develops and implements a non-invasive, low power, portable, functional imaging technology for monitoring brain activity in remote harsh environments, including microgravity. The device uses diffuse optical tomography, which is validated in the project using functional magnetic resonance imaging. Performance on motor tasks of varying complexity under normal and sleep-deprived conditions are conducted with tomographic functional imaging to assess cortical activity in humans during simulated flight tasks, including docking. The technology is also being developed to assess patients with altered intracranial pressure. The sensor work interfaces with a system for automated assessment, warning, and countermeasure evaluation.
Countermeasure Target(s): Physiological and medical monitoring and diagnosis, with countermeasures to adjust scheduling and performance expectations.

Thomas et al.: Diagnostic 3D Ultrasound Algorithms for Space Applications
This project seeks to develop, optimize and validate diagnostic ultrasound in manned space flight, with aims focused on (a) serial 3D examinations to enhance current diagnostic capabilities, (b) utilizing reconstruction and real-time techniques, (c) registering anatomical images from 2D and 3D ultrasound with those obtained from prior ultrasound examination and from magnetic resonance and computed tomographic imaging, (d) abstracting, in an automated

fashion, anatomical changes in ultrasound studies, (e) compression algorithms, and (f) assessing the ability of novice examiners to obtain 3D sonographic data sets (cardiac, renal) following minimal training.
Countermeasure Target(s): Physiological and medical monitoring and diagnosis, with early countermeasure intervention, such as pharmacological agents or nephrolithiasis, when indicated.

Thomas et al.: Echocardiographic Resource for Microgravity Studies
This resource project in ultrasound experimentation and training is a collaboration with the Cardiovascular Alterations team. The goal is to establish an Echocardiographic Core Facility to the NASA research and clinical communities, capable of applying standard and novel analysis techniques in a rigorous fashion to echocardiographic data obtained from selected ground-based experimental models, pre- and post-flight examinations, and eventually from in-flight acquisitions.

Countermeasure Target(s): Physiological and medical monitoring and diagnosis, and training of naïve users in medical image acquisition, with multi-systems applications (e.g., cardiovascular, bone, renal).

The integration activities among the projects just listed, both within the SMST and between the SMST, other NSBRI teams and groups outside the NSBRI, are summarized in Table 12.2. From a technology, modeling and physiological system perspective, the relationships are also illustrated in Figure 12.1. Specifically, each of the eight SMST projects is represented along the middle row of Figure 12.1. The projects are coded to depict (a) NSBRI cross-team interactions (Soller with Cabrera (Nutrition, Physical Fitness and Rehabilitation)), (b) NASA interactions (Davies with Luzod (ARC); Putcha (JSC); Sutton with Marshburn (JSC)), (c) NSBRI cross-team and NASA interactions (Klempner with Fox (Immunology, Infection and Hematology Team) and Pierson (JSC); Thomas with Cohen (Cardiovascular Alterations Team) and JSC)), and (d) none of the above (although Crum has strong ties to the Department of Defense medical technology programs).

The bi-directional arrows in Figure 12.1 represent relationships (a) among projects within the SMST and (b) between SMST projects and the other NSBRI teams. These relationships are broken down into two main categories: Technology; and Physiological Systems and Effects. Across the top row, interactions between SMST projects and the Technology Development Team and core Integrated Human Function activities are shown. These interactions correspond roughly to experimentation (Technology Development Team) and theoretical or modeling (core Integrated Human Function) interactions. Arrows pointing to particular boxes *from* SMST projects *to* boxes in the upper row show how SMST projects contribute to NSBRI developments in other specific domains. For example, the Klempner, Soller and Sutton projects all develop novel spectrographic devices that complement one or more projects being developed in the Technology Development Team (specifically, projects headed by Potember and by Maurer).

Arrows that originate *from* boxes in the upper row of Figure 12.1 and project *to* SMST projects represent links among projects *within* the SMST. The relationships are incomplete and are evolving, sometimes with added benefit to the overall NSBRI scientific program. For example, ultrasound technologies link projects by Crum and Thomas, although Thomas' projects do not develop hardware. The functional magnetic resonance imaging (fMRI) aspects of Sutton's project adds to the (non-functional) MRI developments in the Technology Development Team; hence the half shaded box in Figure 12.1. The chemical engineering and functional genomic and proteomic approaches on the SMST complement other core technology developments within the NSBRI program.

Bi-directional arrows between the boxes representing the SMST projects and the system teams along the bottom row of Figure 12.1 work similarly to those just described. There is synergy with every system team, especially the Cardiovascular Alterations Team. There is also an emerging emphasis on brain and neurobehavioral alterations within the SMST (Sutton project). At present, there is no synergy with the Radiation Effects Team, although there is scientific overlap with that team.

SMST – Technology, Physiological Systems and Interactions

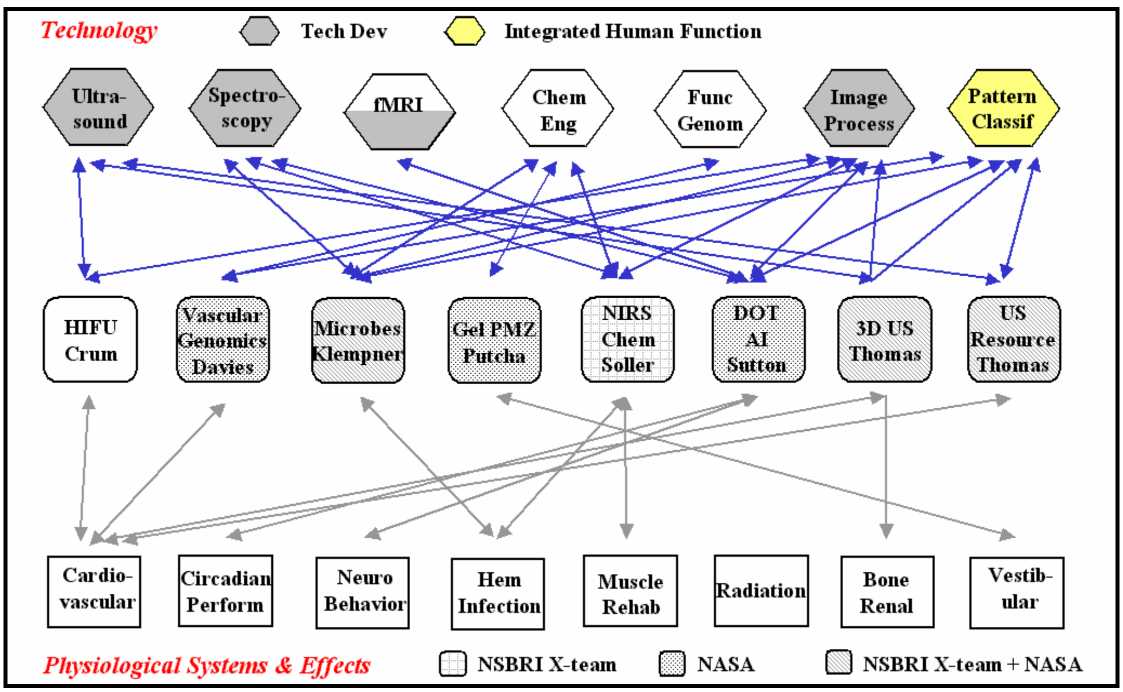

Figure 12.1

In October 2001, the SMST provided a live demonstration of new technologies and added value across projects to the Team Leaders of the other NSBRI teams and to the External Advisory Council. Considerable progress was made by the SMST since October 2001. In March 2002, the Council reported that the SMST:

- "has been remarkably successful in realizing substantial progress and rapid maturation of several of it major projects,"
- "has achieved proof-of-principle or near proof-of-principle countermeasure status of several of the systems within its development domain,"

- "has in many ways succeeded in the fundamental mission of the NSBRI, namely, to engage in basic research that leads to new technologies uniquely suited to the critical needs of NASA space flight demands,"
- "should have as its highest priority the definition of flight-test trajectories for its most successful technologies," and
- "should (have next stage goals that are) highly focused and implemented with a certain sense of urgency" given the team's "success and the current critical stage of development of the NSBRI."

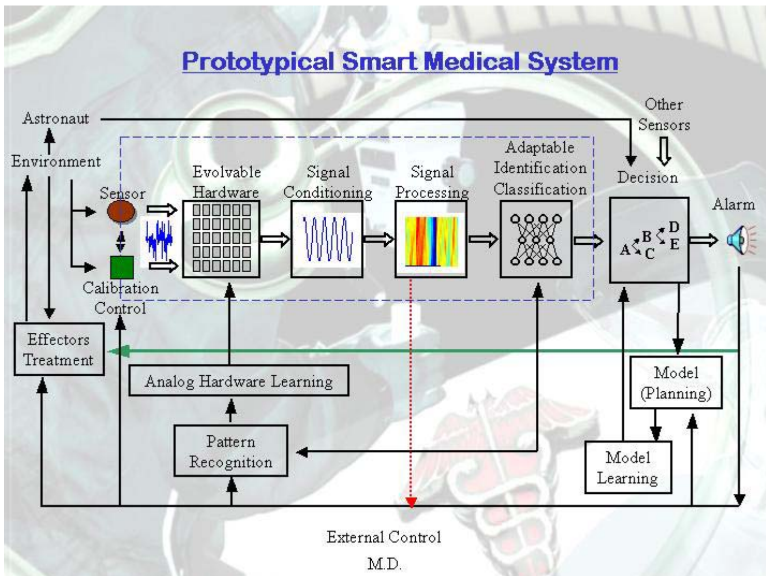

Figure 12.2

To follow through on achieving Goals 1 to 7, the SMST has developed a model prototype and concept of operations to identify gaps, weaknesses, strengths, needs and progress toward mature countermeasures. The model is summarized in Figure 12.2. In this figure, information from the environment and astronauts is sensed by a suite of small, lightweight, low power, portable, non-invasive, unobtrusive, intelligent sensors with pattern recognition capabilities. These sensors feed automatically analyzed, rather than raw, data into decision-making algorithms, that also have cognitive input from the astronauts themselves. There is a model of the system, which is where the NSBRI integration core activities fit into the team's plans. The model not only (a) assesses input from multiple sources, but it (b) pre-plans notification for onboard alarms and information transfer to the ground, (c) looks at contingencies and outcomes for effectors and treatments prior to the administration of countermeasures, (d) assesses the effectiveness of treatments and countermeasures, (e) monitors consequences of actions and countermeasures, and (f) interfaces with models for pattern recognition and analog hardware learning. Since feedback loops exist which are independent of external and M.D. control, the system is, in principle, autonomous. Moreover, the design is achievable, to varying degrees, and proposes a revolutionary new health care system for space, which is central to the research charge assigned to the SMST.

While there are other features of the system described in Figure 12.2, the main points in summary are:

- Enhanced small sensor platforms with pattern recognition and wireless capabilities
- Adaptable system of systems for sensor integration
- Algorithms and models for human assisted monitoring, countermeasure assessment and decision making
- Common platforms for sensing and countermeasure delivery

Tables 12.3a and 12.3b provide projected timelines for achieving Risk-based Goals 1 to 4 using the model of Figure 12.2. Non-risk based Goals 5 to 7 are achieved in parallel to the Risk-based Goals as described in Section 12.5.

12.5 OBJECTIVES AND STRATEGIC ACTIVITIES

The objectives underlying each goal are presented below, along with strategic activities that will be used to achieve the goals and objectives.

Goal 1: Methods to Reduce Risk of Trauma and Acute Medical Problems

<u>Objective 1A</u>. Assess risk and target level of acceptable risk

- Determine the full range of risks to trauma and acute medical problems using evidence based medicine and other approaches. All team members have been acquiring such information from published reports, JSC personnel, and current and former astronauts and flight surgeons.
- Determine the full range of current clinical capabilities taking into account international requirements and resources (Putcha, Klempner, Soller, Sutton, Thomas projects; JSC personnel).

<u>Objective 1B</u>. Determine mechanisms

- Identify technologies suitable for non-invasive physiological assessment (all projects).
- Identify capabilities of sensor technologies for use in trauma (Crum, Soller, Sutton, Thomas projects).
- Identify promising new non-invasive surgical interventions (Crum, Soller, Sutton, Thomas projects).
- Assess validity of sensors based on gold standards in health and disease (Crum, Klempner, Soller, Sutton, Thomas projects).
- Further understanding of signal and effector mechanisms in relation to novel sensor developments (Crum, Soller, Sutton projects).

<u>Objective 1C</u>. Develop countermeasures

- Test sensors for normal anatomical and physiological non-invasive monitoring in animals and humans (Crum, Klempner, Soller, Sutton, Thomas projects).
- Test sensors for anatomical and physiological non-invasive monitoring in animals and humans during trauma and acute medical conditions (Crum, Klempner, Soller, Sutton, Thomas projects).

- Develop time-derivative pattern recognition and other algorithms for near automated detection of significant medical alterations based on sensor data (all projects).
- Refinement of non-invasive surgical capabilities integrated with image guided detection, interpretation and assessment of treatment efficacy (Crum project).
- Human subject demonstration of sensor-algorithm devices for trauma and acute medical problem assessment (Crum, Klempner, Soller, Sutton, Thomas projects).
- Human subject demonstration of sensor-effector (treatment) devices for trauma and acute medical problems (Crum, Soller, Thomas projects).
- Evaluation of sensor-algorithm-effector "smart" system in simulated space flight conditions (e.g., KC135) (Soller, Sutton, Thomas projects).

Goal 2: Methods to Reduce Risk of Toxic Exposure

Objective 2A. Assess risk and target level of acceptable risk

- Determine the full range of risks to toxic exposure based on environmental factors and evidence based medicine from NASA Centers, including JSC, ARC and JPL (e.g., eNose project). Team members have been acquiring such information from published reports, JSC personnel, and current and former astronauts and flight surgeons (Klempner, Sutton projects).
- Determine the full range of current capabilities for management of toxic exposure taking into account international requirements and resources (Klempner, Sutton projects; JSC personnel).

Objective 2B. Determine mechanisms

- Identify emerging technologies suitable for management of toxic exposures in the space environment (Klempner, Sutton projects with input from JSC, ARC and JPL personnel).
- Investigate mechanisms and determine validity of approaches in reducing risk of toxic exposure (Klempner, Sutton projects in collaboration with biotechnology companies, including SRU Biosystems).

Objective 2C. Develop countermeasures

- Test technologies suitable for toxic exposure monitoring in remote harsh environments (Klempner project, collaboration with JSC, ARC biosensors group, JPL).
- Tests sensors on animals for toxic exposures and medical sequelae of exposures (Klempner project, collaboration with JSC, ARC biosensors group, JPL).
- Human subject demonstration of novel technologies for assessment of toxic exposures (Klempner project, collaboration with JSC and ARC biosensors group).
- Evaluation of "smart" systems for assessment of toxic exposure in simulated space environment (Klempner, Sutton projects, collaboration with JSC personnel).

Goal 3: Methods to Reduce Risk of Altered Pharmacodynamics and Adverse Drug Reactions

Objective 3A. Assess risk and target level of acceptable risk

- Determine the full range of risks and implications of space flight alterations in human physiology concerning pharmacology for clinically useful medications. This requires

interactions with JSC scientists, flight surgeons and astronauts. Team members have been acquiring such information (Klempner, Putcha, Sutton, Thomas projects).
- Determine the full range of current pharmacological practices taking into account international requirements and resources (Putcha project; JSC personnel).

Objective 3B. Determine mechanisms
- Identify emerging technologies suitable for establishing the effects and implications regarding absorption, distribution, metabolism, clearance, excretion, clinical efficacy, side effects and drug interactions for clinically useful medications (Putcha, Sutton, Thomas projects).
- Investigate mechanisms and determine validity of approaches for quantifying altered pharmacodynamics and adverse drug reactions (Putcha project; this area requires further support).

Objective 3C. Develop countermeasures
- Test technologies suitable for non-invasive drug delivery of clinically relevant medications for space flight (Putcha project).
- Establish clinical efficacy and side effect profiles of appropriate medications for space flight (Putcha project).
- Determine space and radiation hardness of appropriate medications (this area requires further support).
- Human subject demonstration of novel drug delivery system with established efficacy and high benefit to risk ratio (Putcha project in collaboration with JSC flight surgeons and astronauts).

Goal 4: Methods to Reduce Risk of Illness and Ambulatory Health Problems

Objective 4A. Assess risk and target level of acceptable risk
- Determine the full range of risks of illnesses and ambulatory health problems using evidence based medicine. All team members have been acquiring such information from published reports, JSC personnel (in collaboration with the Director of the Space and Life Sciences Directorate) and current and former astronauts and flight surgeons.
- Determine the full range of current clinical capabilities taking into account international requirements and resources (Crum, Klempner, Putcha, Soller, Sutton, Thomas projects; JSC personnel).

Objective 4B. Determine mechanisms
- Identify emerging technologies suitable for management of illnesses and ambulatory health problems in the space environment (Crum, Klempner, Putcha, Soller, Sutton, Thomas projects).
- Investigate mechanisms and determine validity of approaches in reducing risk of illness and ambulatory health problems (Crum, Klempner, Putcha, Soller, Sutton, Thomas projects).

Objective 4C. Develop countermeasures
- Test technologies suitable for conducting a nominal health and fitness examination, and for performing ongoing health monitoring, in remote harsh environments (Crum, Klempner, Putcha, Soller, Sutton, Thomas projects).

- Tests sensors on animals for physiological monitoring (Crum, Klempner, Putcha, Soller, Thomas projects).
- Human subject demonstration of novel technologies for assessment of nominal health and fitness examination, and ongoing health monitoring, in simulated space environment (Crum, Klempner, Putcha, Soller, Sutton, Thomas projects).
- Evaluation of "smart" systems for assessment of nominal health and fitness examination, and ongoing health monitoring, in simulated space environment (Crum, Klempner, Putcha, Soller, Sutton, Thomas projects).

Goal 5: Develop a Platform for Suite of Medical Devices

Objective 5A Assess and develop platform prototypes

- Identify adaptable, reconfigurable hardware that is software intense and able to support a suite of medical devices (Crum, Klempner, Sutton, Thomas projects; this area requires further support).
- Develop software capable of providing local computation on sensors with integrative abilities across the entire suite of sensors (Sutton project; this area requires further support).
- Develop models of the entire network that can process data streamed in real-time, predict outcomes and recommend actions, including countermeasure delivery (Sutton project; this area requires further support).

Objective 5B. Implement platforms and assess capabilities

- Test hardware and software prototypes by adding a single sensor-algorithm-effector system to the platform and ensuring that the system remains functional (Crum, Davies, Klempner, Sutton, Thomas projects; this area requires further support).
- Add several sensor-algorithm-effector systems to the platform and ensure that each system remains functional (Soller, Sutton projects; this area requires further support).
- Link systems to provide added value to physiological monitoring, prediction and countermeasure delivery (Sutton project in collaboration with JSC medical operations; this area requires further support).
- Expand system to automate monitoring and countermeasure delivery in significant risk scenarios, including trauma, toxic exposure, illness and ambulatory health problems (Crum, Soller, Sutton projects in collaboration with JSC medical operations; this area requires further support).

Goal 6: Develop Earth-based Applications for Non-invasive, Portable Physiological Sensing and Medical Diagnostic and Therapeutic Devices

Objective 6A. Identification and demonstration

- Identify promising developments within and between projects, and identify the need(s) for applying these developments to Earth-based problems (all team projects).
- Demonstrate promise of efficacy and superiority of technologies to solve Earth-based problems (all team projects).

Objective 6B. Leveraging and transition

- Secure additional support from government, academic and/or industry to leverage NSBRI funding and to firmly establish efficacy and superiority of technologies to solve Earth-based problems (all team projects).

- Protect intellectual property.
- Engage NSBRI Industry Forum and other avenues to perform due diligence and possible commercialization.

Goal 7: Integrate Research and Analysis

Objective 7A. Integrate research within the Smart Medical Systems Team

- Continue current integration efforts among team PIs, co-investigators and key NASA personnel affiliated with team projects, as summarized in Table 12.2.

Objective 7B. Integrate research with other teams

- Continue current integration efforts with other teams and with integrated human function modeling efforts, as summarized in Figure 12.1.
- Continue coordinated technology development efforts with the Technology Development Team.
- Continue coordinated interactions and collaborations with the Cardiovascular Alterations, Human Performance Factors, Sleep and Chronobiology, Neurobehavioral and Psychosocial Factors, Immunology, Infection and Hematology, Muscle Alterations and Atrophy, Nutrition, Physical Fitness and Rehabilitation, Bone Loss and Neurovestibular Adaptation Teams (mapping of SMST projects to other teams shown in Figure 12.1).
- Coordinate with the Radiation Team regarding the effects of space radiation on medical illness in animals as a prelude to assessing and monitoring the effects in humans.

Objective 7C. Integrate research with investigators not formally associated with the NSBRI

- Although all of the projects on the SMST involve collaborations among leading investigators from different schools, universities, companies and Federal agencies, team members continue to seek out expertise from scientists not formally part of the NSBRI who can contribute to many of the areas under study. The number of investigators who initially were not associated with the NSBRI and who now collaborate with the SMST exceeds the number of investigators originally supported on the team. The SMST continues to serve as a nidus in an emerging area of space and Earth-based biomedical research.

12.6 SUMMARY

The SMST is a collaborative effort within the NSBRI and with NASA that firmly embraces the countermeasure development paradigm to deliver critical aspects of an advanced, integrated and autonomous system for astronaut health assessment, maintenance and medical care. The success of the team is dependent upon new enabling technologies, the establishment of risk priorities based on hard evidence and opportunities to demonstrate countermeasure efficacy on the ground and in a space medicine environment. The importance of this research is clear, as the risk of Trauma and Acute Medical Problems is one of the four Type I risks on the Critical Path Roadmap. The team currently focuses on the top four out of six risks (Risk-Based Goals 1 to 4) listed under Clinical Capabilities in the Critical Path Roadmap. Modeling and applications for Earth-based care are active areas of investigation and achievement.

Tables 12.3a and 12.3b summarize the plans to achieve Goals 1 to 4. While there is a critical mass of investigators to implement this plan, there is a need to supplement the work in pharmacology and in the systems engineering to develop a platform for a smart medical system. Moreover, it should be recognized that further support is required to foster the critical interface between members of the SMST and the flight surgeon and NASA engineering communities, especially with respect to meeting medical requirements and achieving feasible device implementation.

With adequate adjustment in program support, it is anticipated that the SMST will continue its successful course as noted by the External Advisory Council in March 2002. There is enormous potential in the team's individual projects, the added value across team projects and interactions with other teams. The SMST is well positioned to make significant contributions to Earth-based clinical care. Figure 12.1 summarizes the implemented strategy for interactions and Figure 12.2 proposes the strategic model for a revolutionary form of a smart medical system for space and for Earth.

National Space Biomedical Research Institute
SMART MEDICAL SYSTEMS PROGRAM

Table 12.1. Project Research Activities

PI/Project	Risk(s) Addressed	Countermeasure Target	Experimental System	Phase 1 Activities: Focused Mechanistic Research	Phase 2 Activities: Preliminary Countermeasure Development Research	Phase 3 Activities: Mature Countermeasure Development Research
CRUM/Guided High Intensity Focused Ultrasound for Mission-Critical Care	Trauma, acute medical problems	Monitoring, med assessment Surgery	Image guided HIFU for acoustic hemostasis	Determine efficacy of HIFU on tissue for bloodless surgery	Develop integrated imaging – HIFU system	Planning for human demonstration of system
DAVIES/ Vascular Genomics in Gravitational Transitions	Rehabilitation following landing	Training	Hypergravity mice, vascular RNA	Understand vascular gene, protein effects in hyper-g		
KLEMPNER/Smart Medical System for Microorganism Detection	Trauma, acute med Toxic exposure Illness, ambulatory health problems	Monitoring, med assessment Pharmacological agents	Phage displayed ligands Colorimetric resonant sensors	Establish microbial phage libraries of space fungi and sensitivity of reflectance biosensor	Develop and test novel sensor to detect and analyze phages	
PUTCHA/Microcapsule Gel Formulation for Intranasal Promethazine	Altered pharmacodynamics	Pharmacological agents	Microencapsulation Kinetics and bio-availability in rat		Develop and test microencapsulated promethazine	Planning of human studies for drug delivery system

SOLLER/Noninvasive Measurement of Blood and Tissue Chemistry	Trauma, acute med Illness, ambulatory health problems	Monitoring, med assessment Exercise	Near infra-red spectroscopy and algorithms	Refine NIRS technology for tissue pH and hematocrit determination	Utilize NIRS for non- invasive tissue moni-toring during exercise	
SUTTON/Near Infrared Brain Imaging for Space Medicine	Trauma, acute med Illness, ambulatory health problems	Monitoring, med assessment Performance adjustments	Diffuse optical tomography, simulated docking task, ICP changes	Develop DOT system and validate using fMRI to detect regional brain activity and ICP changes	Integrate DOT assessment of brain function during simulated docking task	
THOMAS/Diagnostic 3D Ultrasound Algorithms for Space Applications	Trauma, acute med Illness, ambulatory health problems	Monitoring, med assessment Pharmacological agents	Ultrasound and algorithms in animal and human models	Identify and adapt new algorithms for real-time evaluation of cardiac and renal echo data	Develop and test algorithms for semi-automated interpretation	
THOMAS/Echocardiograp hic Resource for Microgravity Studies	Trauma, acute med Illness, ambulatory health problems	Monitoring, med assessment Training	Training paradigms		Testing of training protocols to use echo equipment and analyze	Plans to test system during space flight

National Space Biomedical Research Institute
SMART MEDICAL SYSTEMS PROGRAM

Table 12.2. Integration Activities

	CRUM HIFU for mission critical care	**DAVIES** Vascular genomics in g transitions	**KLEMPNER** Smart microorganism detection sys	**PUTCHA** Microcapsule drug formulation	**SOLLER** Non-invasive blood & tissue chemistry	**SUTTON** Near infrared brain imaging for space med	**THOMAS** Diagnostic 3D ultrasound for space	**THOMAS** Echo-cardiographic resource
Internal Communication	Monthly team telecon; Biannual team meeting; NSBRI retreat; Biannual NASA meeting; National scientific meetings	Monthly team telecon; Biannual team meeting; NSBRI retreat; Biannual NASA meeting; National scientific meetings	Monthly team telecon; Biannual team meeting; NSBRI retreat; Biannual NASA meeting; National scientific meetings	Monthly team telecon; Biannual team meeting; NSBRI retreat; Biannual NASA meeting; National scientific meetings	Monthly team telecon; Biannual team meeting; NSBRI retreat; Biannual NASA meeting; National scientific meetings	Monthly team telecon; Biannual team meeting; NSBRI retreat; Biannual NASA meeting; National scientific meetings	Monthly team telecon; Biannual team meeting; NSBRI retreat; Biannual NASA meeting; National scientific meetings	Monthly team telecon; Biannual team meeting; NSBRI retreat; Biannual NASA meeting; National scientific meetings
Integrated Experiment Development	Sensor aspects link to both THOMAS projects	Vascular studies link Cardiovascular Alterations team	Algorithms link to SUTTON project; Phage library studies link to IIH team	Promethazine development links to Neurovestibular Adaptation team	Sensor links to SUTTON project; Applications links to Muscle team	Sensor links to SOLLER project; Algorithms link to KLEMPNER and THOMAS projects	Sensor links to CRUM project; Algorithms link to SUTTON project; Echo links to CV team	Sensor links to CRUM project; Algorithms link to SUTTON project; Echo links to CV team

Sample Sharing			Specimen sharing with JSC microbiology		Collaboration with CABRARA project	Cognitive task sharing with JSC flight surgeons	Vascular investigations link to DAVIES project	Resource is shared within NSBRI and NASA
Synergistic Studies of Opportunity	Studies with DoD / DARPA	Bioengineering Center, U Penn	SRU Biosystems, biotechnology industry	Pharma industry collaborations	Medical assessment for diabetics, surgical patients	Neuro monitoring in ICU, Harvard	Cardiac, renal imaging apps in med practice; flight apps	Resource of National value
Development of Computer Model of Integrated Human Function	Image / model guided surgery	Data mining	Neural nets for pattern recognition		Algorithms for pattern identification	Neural nets, software engineering platform	Algorithms for individualized astronaut models	Modeling for training purposes

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Table 12.3a. Achieving Goal 1: Methods to Reduce the Risk of Trauma and Acute Medical Problems

Countermeasure Development Phases	Pre 2001	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Phase 0: Observational & Phenomenological Research													
Phase 1: Focused Mechanistic Research													
• Identify technologies suitable for non-invasive physiological assessment • Identify capabilities of sensor technologies for use in trauma • Identify promising new non-invasive surgical interventions • Assess validity of sensors based on gold standards in health and disease • Establish with NASA Medical Ops personnel levels of risks in humans													
Phase 2: Preliminary Countermeasure Development Research													
• Test sensors for normal anatomical and physiological non-invasive monitoring in animals and humans													
• Test sensors for anatomical and physiological non-invasive monitoring in animals and humans during trauma and acute medical conditions • Develop time-derivative pattern recognition and other algorithms for near automated detection of significant medical alterations based on sensor data • Refinement of non-invasive surgical capabilities integrated with image guided detection, interpretation and assessment of treatment efficacy													

Phase 3: Mature Countermeasure Development Research													
• Human subject demonstration of sensor – algorithm devices for trauma and acute medical problem assessment													
• Human subject demonstration of sensor – effector (treatment) devices for trauma and acute medical problems													
Phase 4: Countermeasure Evaluation & Validation													
• Evaluation of sensor – algorithm – effector "smart" system in simulated space flight conditions													
Phase 5: Operational Implementation of Countermeasure Strategy													

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Table 12.3b. Achieving Goals 2-4: Methods to Reduce the Risk of Toxic Exposure, Altered Pharmacodynamics and Adverse Drug Reactions, and Illness and Ambulatory Health Problems

Countermeasure Development Phases	Pre 2001	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Phase 0: Observational & Phenomenological Research													
Phase 1: Focused Mechanistic Research													
• Identify emerging technologies suitable for management of toxic exposures, drug delivery and alterations, and nominal health exam, in space environment • Investigate mechanisms and determine validity of approaches in health problems • Establish with NASA Medical Ops personnel levels of risks in humans													
Phase 2: Preliminary Countermeasure Development Research													
• Test technologies suitable for health monitoring in remote harsh environments													
• Test sensors for toxic exposures and medical sequelae of exposures • Investigate novel drug delivery and other pharma concerns to reduce drug adversity in space environment													
Phase 3: Mature Countermeasure Development Research													
• Human subject demonstration of novel technologies for assessment of health and medical problems, including exposure to toxins • Determine in human trials countermeasure effectiveness of new pharma approaches relevant for space													
Phase 4: Countermeasure Evaluation & Validation													
• Evaluation of "smart" systems for assessment of health and medical problems in simulated space flight conditions • Establish efficacy of new pharma approaches, including microencapsulation													
Phase 5: Operational Implementation of Countermeasure Strategy													